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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,670	05/02/2001	Barry C. Finzel	6263.N	4815

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,670	FINZEL ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *1-37 and 44-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-48* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

DETAILED ACTION

Applicants' election with traverse of Group IX (claims 38-43) as set forth in Paper No. 8, filed 10/16/02, is acknowledged. Claims 1-37 and 44-48 are withdrawn from consideration due to the claims being drawn to non-elected Groups.

The traversal to withdrawing the restriction requirement between Groups VIII, IX, and XI was found unpersuasive because of the following reasons (summarized from the restriction paper):

The inventions are distinct, each from the other because they are directed to different chemical types regarding the critical limitations therein. For Group VIII, the critical feature is a crystallization methodology of Hepatitis C virus helicase. For Groups IX and XI, the critical feature is a crystalline Hepatitis C virus helicase and incorporation of a chemical entity in a crystal. respectively.

Inventions in Groups IX-XI are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the crystalline Hepatitis C virus helicase of Group IX may be utilized in distinct usages as needed in Group X for a method of solving a crystal structure of a crystal, in a method for incorporating a chemical entity in a crystal as in Group XI, or alternatively, in detecting a disease. All of these usages are distinct as requiring distinct and different functions

thereof without overlapping search due to different subject matter. This lack of overlapping searches documents the undue search burden if they were searched together.

The requirements are still deemed proper and are therefore made FINAL.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to crystals, crystallographic structure, and methods whereas in contrast the elected claims do not contain methods.

The information disclosure statement (IDS) filed 11/14/02 does comply, however the IDS filed 1/31/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The list of references in the IDS, filed 1/31/02, has been placed in the application file, but the information referred to therein has not been considered. If Applicants desire the IDS filed 1/31/02 to be considered during examination on the merits, then a copy of the references must be supplied when the next response is filed to this Office Action.

Applicant is hereby notified that the required timing for the correction of drawings has changed. See the last 6 lines on the sheet which is attached titled "Attachment for PTO-948 (Rev. 03/01 or earlier)". It is noted that a PTO Form 948 is mailed herewith. Due to the above notification Applicant is required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

Claims herein under examination are claims 38-43.

Specification

The disclosure is objected to because of the following informalities: "inhibotors" is misspelled on page 7, line 18; "becasue" is misspelled on page 16, line 30: and "teh" is misspelled on page 49, line 1. Appropriate correction of these and any other spelling errors is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 26, line 10. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 42 is objected to because of the following informality: as written, the grammatical structure of the claim is awkward, particularly in the manner of using words "having" and "is". Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 42 and 43 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Although Applicants have disclosed information to enable one skilled in the art to make the tetragonal and orthorhombic crystals of crystalline Hepatitis C virus helicase with unit cell dimensions a = b = 109 Å ± 3 Å; c = 84 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P4_1$ as well as a = 66 Å ± 2 Å; b = 110 Å ± 3 Å; c = 64 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P2_12_12$, respectively, the specification does not reasonably provide

enablement for other crystalline Hepatitis C virus helicases and compositions comprising the same as stated in claims 42 and 43. The claims are broader than the enablement provided by the disclosure with regard to the large number of possible crystalline helicases that could be made. As the science of protein crystallization is well known to be a trial and error procedure with unpredictable results (Drenth, page 1, lines 13-20), one skilled in the art would require clear and precise guidance to make any particular crystal. Accordingly, it would be very difficult for a skilled artisan to make crystal structures of other crystalline Hepatitis C virus helicases or co-complexes beyond those mentioned in the instant case where specific coordinates are disclosed. Due to the unpredictability and difficulty of crystallizing proteins, it is unlikely that one of skill in the art would be able to make another crystal relying solely on the information for the two crystals disclosed in the specification without undue experimentation. Also, the information provided in Examples 4 and 5, pages 49-50, does not sufficiently enable a skilled artisan to make compositions comprising crystalline Hepatitis C virus helicase as no specific chemical entities or ligands were mentioned. Again, due to the unpredictability in the art, a skilled artisan could not reasonably expect to make such co-crystalline complexes based on generic guidelines without undue experimentation.

LACK OF WRITTEN DESCRIPTION

Claims 38-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38-43 are directed to crystalline Hepatitis C virus helicases and compositions comprising the same. There is no disclosure regarding any crystals other than the tetragonal crystal having unit cell dimensions of a = b = 109 Å ± 3 Å; c = 84 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P4_1$ as well as the orthorhombic crystal having unit cell dimensions of a = 66 Å ± 2 Å; b = 110 Å ± 3 Å; c = 64 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P2_12_12$. Open claim language, such as "comprising" (claims 38, 40, and 43 and dependent claims 39 and 41 therefrom) and "having" (claims 38 and 42 and dependent claims 39 and 43 therefrom), suggests the claims may contain other crystals which do not meet the written description provision of 35 USC 112, first paragraph. Applicants have not sufficiently described other crystals and compositions in such full, clear, and concise terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

The specification discloses SEQ ID NO: 1 which corresponds to an amino acid sequence of Hepatitis C virus helicase. SEQ ID NO: 1 and its complement of the same length meet the written description provisions of 35 USC 112, first paragraph. However, due to the facts that "having" (claim 42) and "comprising" (claim 43) are open claim language and the phrase "*the/an* amino acid sequence" (claims 39, 41, and 42, and dependent claim 43 therefrom) may contain the entire sequence or just a fragment of the sequence, these claims are directed to encompass such amino acid sequences described above. None of these sequences, other than SEQ ID NO: 1 and its full complement of the same length, meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 12, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 1, its full length complement, and the specifically mentioned crystals, but not the full breadth of claims 38-43 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39, 41, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39 and 41 recite the phrase "*the* amino acid sequence" which is vague and indefinite. It is unclear whether the sequence is referring to the entire sequence or just a fragment of the sequence. Claim 42 is also rejected due to its dependency from claims 39 and 41.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (1998). As "having an amino acid sequence" is open claim language as well as undefined regarding the inclusion of the entire sequence or an unlimited selection of fragments, Kim et al. disclose a crystalline Hepatitis C virus helicase with an amino acid sequence (Figure 5) (amino acid residues 1359-1474) that identically matches a fragment of SEQ ID NO: 1 (amino acid residues 168-283). The helicase disclosed by Kim et al.

encompasses a composition as stated in claim 43. Therefore, Kim et al. teach all of the limitations of claims 42 and 43.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 19, 2002

ARDIN H. MARSCHEL
PRIMARY EXAMINER

Continuation of Attachment(s) 6). Other: Sequence match listing (2 pages).